

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 November 2004 (11.11.2004)

PCT

(10) International Publication Number
WO 2004/096846 A3

(51) International Patent Classification⁷: **C07K 14/47**,
C12N 15/12, C07K 16/18

(21) International Application Number:
PCT/US2004/012354

(22) International Filing Date: 23 April 2004 (23.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/465,149 24 April 2003 (24.04.2003) US

(71) Applicants and

(72) Inventors: **SESSA, William, C.** [US/US]; 4 Richborough
Rd., Madison, CT 06443 (US). **ACEVEDO, Lisette**
[US/US]; 750 Whitney Ave., #B7, New Haven, CT 06511
(US).

(74) Agents: **HALEY, James, F., Jr.** et al.; Fish & Neave, 1251
Avenue of the Americas, New York, NY 10020 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

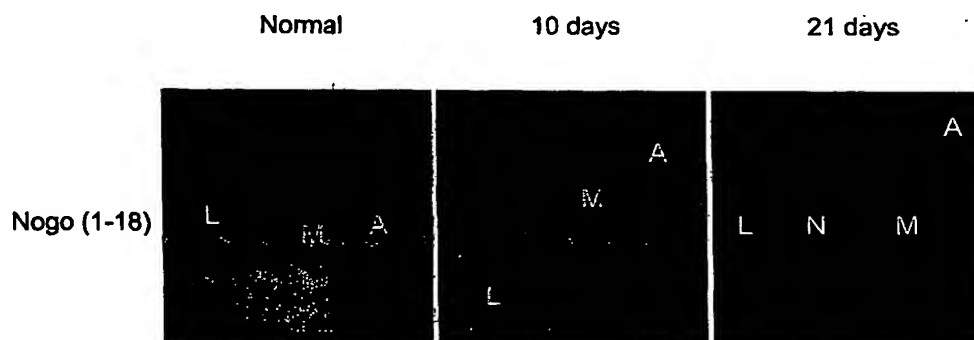
— with international search report

(88) Date of publication of the international search report:
27 January 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **NOGO-B, A REGULATOR OF ENDOTHELIAL CELL FUNCTION AND VESSEL REMODELING**

Nogo expression decreases after injury and by 21 days is almost completely gone from vessel wall



(57) Abstract: The present invention relates to previously unknown biological roles of Nogo-B. We have discovered that Nogo-B is a component of endothelial cells. We have also discovered that Nogo-B is highly expressed in intact blood vessels. The amino terminus of Nogo-B promotes the adhesion, spreading and migration of endothelial cells and plays a role in vascular remodeling. Thus, Nogo-B is a novel regulator of vascular homeostasis and remodeling. The present invention provides compositions comprising Nogo-B and fragments and fusion proteins thereof. The present invention also relates to nucleic acids encoding Nogo-B and fragments and fusion proteins thereof, as well as vectors and cells comprising such nucleic acids. The present invention also relates to antibodies specific for Nogo-B and fragments and fusion proteins thereof. The present invention also provides methods for preventing, detecting and treating Nogo-B-related diseases, disorders and conditions.

INTERNATIONAL SEARCH REPORT

ational Application No
/US2004/012354

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/47 C12N15/12 C07K16/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/60083 A (CHIRON CORP) 12 October 2000 (2000-10-12) SEQ ID NOs:1 and 2 claims 1-5,10-13,17,20	1-6,8,9, 15-27, 30-32
X	PRINJHA R ET AL: "Inhibitor of neurite outgrowth in humans" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 403, 27 January 2000 (2000-01-27), pages 383-384, XP002144397 ISSN: 0028-0836 the whole document -/--	1-6,8,9, 15-22

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

28 September 2004

Date of mailing of the international search report

25/10/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Herrmann, K

INTERNATIONAL SEARCH REPORT

ational Application No

/US2004/012354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	-& DATABASE EMBL 22 July 2000 (2000-07-22), XP002298205 retrieved from NCBI Database accession no. AJ251384 the whole document	1-6
X	----- WATARI A ET AL: "Multi-functional gene ASY/Nogo/RTN-X/RTN4: Apoptosis, tumor suppression, and inhibition of neuronal regeneration." APOPTOSIS, vol. 8, no. 1, January 2003 (2003-01), pages 5-9, XP002298201 ISSN: 1360-8185	1-6
A		8,9, 15-27, 30-32, 38-45, 49-54
X	----- GOLDBERG J L ET AL: "Nogo in nerve regeneration" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 403, 27 January 2000 (2000-01-27), pages 369-370, XP002967280 ISSN: 0028-0836	1-6
A		8,9, 15-27, 30-32, 38-45, 49-54
X	----- LI QIN ET AL: "Link of a new type of apoptosis-inducing gene ASY/Nogo-B to human cancer" ONCOGENE, vol. 20, no. 30, 5 July 2001 (2001-07-05), pages 3929-3936, XP002298202 ISSN: 0950-9232	1-6
A		8,9, 15-27, 30-32, 38-45, 49-54
	----- -/-	

INTERNATIONAL SEARCH REPORT

International Application No

/US2004/012354

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	OERTLE THOMAS ET AL: "Do cancer cells die because of Nogo-B?" ONCOGENE, vol. 22, no. 9, 6 March 2003 (2003-03-06), pages 1390-1399, XP002298203 ISSN: 0950-9232	1-6
A		8,9, 15-27, 30-32, 38-45, 49-54
P,X	----- ACEVEDO LISETTE ET AL: "A new role for Nogo as a regulator of vascular remodeling" NATURE MEDICINE, vol. 10, no. 4, April 2004 (2004-04), pages 382-388, XP002298204 ISSN: 1078-8956 published online 21 March 2004 the whole document -----	1-6,8,9, 15-27, 30-33, 38-45

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/012354

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 7, 10-14, 28, 29, 34-37, 46-48 and partially claim 38
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 33 and 38-54 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 7, 10-14, 28, 29, 34-37, 46-48 and partially claim 38
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 33 and 38-54 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: 7, 10-14, 28, 29, 34-37, 46-48 and partially claim 38

Claim 10 fails to comply with the requirements of Art. 6 PCT (clarity) to such an extent that a meaningful search could not be carried out (Art. 17(2)(a)(ii) PCT). No detectable labels are defined.

Compounds as such are not sufficiently defined by their mode of action. Therefore, claims 7, 11-14, 28, 29 and 46-48 have not been searched because a Nogo-B agonist or a Nogo-B antagonist is neither disclosed nor supported within the terms of Art. 5 and 6 PCT, respectively (Art. 17(2)(a)(ii) PCT).

Compounds as such are not sufficiently defined by their mode of action. Therefore, claims 34-37 have not been searched because a nucleic acid molecule comprising a nucleotide sequence encoding the heavy chain or the light chain of an antibody or portion thereof that specifically binds to Nogo-B or an antigen-binding portion thereof is neither disclosed nor supported within the terms of Art. 5 and 6 PCT, respectively (Art. 17(2)(a)(ii) PCT).

Claim 38 covers all molecules having the desired characteristic of binding Nogo-B. However, the application provides support (Art. 6 PCT) and disclosure (Art. 5 PCT) for only a limited number of such molecules. Thus, a meaningful search over the whole of the scope claimed is impossible. Consequently, the search has been limited to antibodies that bind Nogo-B (cf. Art. 17(2)(a)(ii) PCT).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

/US2004/012354

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 0060083	A	12-10-2000	AU	4216200 A	23-10-2000
			WO	0060083 A1	12-10-2000